REMARKS

I. Status of the claims

Claims 1-15 and 20-25 are pending in this application. Claims 1-10, 20, and 21 were elected in response to the Restriction Requirement of May 29, 2008. Claims 11-15 and 22-25 have been withdrawn by the Office for being directed to non-elected subject matter. No claim has been amended in this response.

II. Priority

The Office indicated that Applicants have not filed a certified copy of the priority application as required by 35 U.S.C. 119(b). Office Action at 4. Applicants point out, however, that a certified copy of the priority application was filed with the International Bureau during the PCT stage of this application under PCT rule 17. The International Bureau in turn provided the USPTO with a copy of the priority application, whose receipt was acknowledged in the Notification of Defective Response dated November 28, 2006. This notification listed the priority document as one of the items that the USPTO had received as a designated/elected Office. Accordingly, Applicants believe they have complied with the requirements of 35 U.S.C. 119(b) necessary to receive the corresponding benefit of priority. However, upon request by the Office, Applicants will submit another certified copy of the priority application if this document has been misplaced or is otherwise no longer available to the Office.

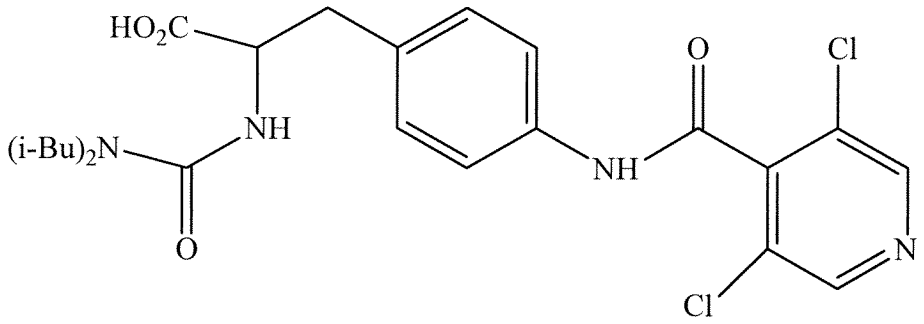
III. Rejections under 35 U.S.C. § 103

The Office rejected claims 1-10, 20 and 21 under 35 U.S.C. 103(a) as being obvious over WO 2002/014272 (a caplus abstract and the whole reference) in view of

Patani and LaVoie, Bioisoterism: A rational approach in drug design, *Chem. Rev.* 96:3147-3176 (1996) ("*Patani.*") Office Action at 5.

a. The Office's rejection

According to the Office, WO 2002/014272 teaches the following compound as a VLA-4 antagonist (the caplus abstract lists this compound as "compound 401470-74-4"):



Office Action at 6. The Office states that *Patani* teaches that sulfone (-SO_2-) is a bioisostere of the carbonyl group. *Id.* The Office argues that *Patani* teaches "that sulfone moieties have been increasingly used as bioisosteres, and that the greater size associated with the sulfone moiety has been shown to be a factor that modulates biological activity." *Id.* (citing *Patani* at 3167).

The Office concludes that "[o]ne of ordinary skill would be motivated, from the disclosure in the prior art, to make the modification required to arrive at the instant invention with reasonable expectation of success for obtaining a compound with the same activity." *Id.* In support of this rationale, the Office quotes an entire section from the M.P.E.P. directed to the "obvious to try" portion of the obviousness guidelines issued after the *KSR* Supreme Court decision (M.P.E.P. § 2143.E). Applicants respectfully traverse this rejection.

b. Applicants respectfully request a translation of WO 2002/014272

Applicants point out that WO 2002/014272 is a publication in the Japanese language for which the Office has provided no translation. Although the Office cited a caplus abstract identifying compound 401470-74-4, Applicants have been unable to determine the specific portion of WO 2002/014272 that discloses compound 401470-74-4. Compound 401470-74-4 does not seem to be any of the compounds disclosed in tables 1 to 5 of WO 2002/014272. Also, the activity of compound 401470-74-4 in the inhibition of VLA-4/VCAM-1 adhesion does not seem to be reported in table 6 of the reference. Respectfully, Applicants would like to request an English-language translation of WO 2002/014272 pursuant to the guidelines for examination from the M.P.E.P.:

> If the document [used in a rejection] is in a language other than English and the examiner seeks to rely on that document, *a translation must be obtained so that the record is clear* as to the precise facts the examiner is relying upon in support of the rejection. The record must also be clear as to whether the examiner is relying upon the abstract or the full text document to support a rejection. The rationale for this is several-fold. It is not uncommon for a full text document to reveal that the document fully anticipates an invention that the abstract renders obvious at best. The converse may also be true, that the full text document will include teachings away from the invention that will preclude an obviousness rejection under 35 U.S.C. 103, when the abstract alone appears to support the rejection.

M.P.E.P. § 706.02.II (italics added). As explained in the above passage, and as will be shown below, the nature of the disclosure in WO 2002/014272 regarding compound 401470-74-4 is relevant to the obviousness analysis of the pending claims. Accordingly, in addition to requesting an English-language translation of WO 2002/014272, Applicants respectfully request that the Office point out the portion of

WO 2002/014272 that discloses compound 401470-74-4, or which otherwise forms the basis of the instant rejection.

c. To establish obviousness of a new chemical compound, the law requires that the Office identify not only a lead compound, but also a reason to modify such compound in a particular manner

In a recent decision addressing the standard for obviousness of chemical compounds, the Federal Circuit interpreted the KSR decision as "assum[ing] a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions." *Eisai Co., Ltd. v. Dr. Reddy's Laboratories*, No. 2007-1397, 1398, slip op. at 8 (Fed. Cir. 2008). Applying this assumption to chemical cases, the court concluded that "post-*KSR*, a prima facie case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound." *Id.*

Moreover, once a suitable starting point has been established, there must also be "a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention.'" *Takeda Chem. Ind., Ltd. v. Alphapharm Pty., Ltd.*, 83 U.S.P.Q.2d 1169, 1174 (Fed. Cir. 2007) (citations omitted). Thus, "in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new compound." *Id.* (underlining added).

These recent decisions require that the Office: a) identify a compound that would have been considered by one of ordinary skill in the art as suitable for further

modification, and b) explain the reasons why such skilled artisan would have made the specific modifications proposed by the Office to arrive at the claimed invention.

Moreover, even under the "obvious to try" rationale advanced by the Office in this rejection, it remains necessary that one of ordinary skill in the art would have had "a reasonable expectation of success" in making the modifications proposed by the Office. M.P.E.P. § 2143.E. As will be shown below, the Office has not complied with any of the above requisites.

d. The Office has not shown that compound 401470-74-4 would have been considered a suitable compound for further modification by one of ordinary skill in the art

The Office has provided no reason why a skilled artisan would have chosen compound 401470-74-4 as a starting material for the modification the Office suggested. The Office has not cited to any portions of WO 2002/014272 that would have led one of ordinary skill in the art to choose compound 401470-74-4 for further modification. WO 2002/014272 discloses at least 37 different specific compounds (see tables 1 to 5). However, upon review of WO 2002/014272, Applicants could not find any specific reference to compound 401470-74-4 that would have singled it out from among all other compounds disclosed. This is specially true given that Applicants could not find compound 401470-74-4 in Table 6, which reports the results of an inhibition assay performed with various compounds, and which indicates the relative inhibitory activity of each of the compounds tested.

For at least this reason, the Office has not met the requirements of a prima facie case of obviousness and Applicants respectfully request that this rejection be withdrawn.

e. Independently of the legal standard, one of ordinary skill in the art would not have combined the teachings of *Patani* and WO 2002/014272

The Office argues that *Patani* teaches "that sulfone moieties have been increasingly used as bioisosteres" of the carbonyl group. Office Action at 6. However, *Patani* only suggests "modification of lead compounds." *Patani* at page 3147, col. 2 (underlining added). That is, the teachings of *Patani* are applicable once one of ordinary skill in the art has identified a suitable compound as a lead compound for modification in order to obtain "safer and more clinically effective agents." *Id.*

Therefore, independently of the legal requirements imposed by the Federal Circuit in an obviousness analysis, one of ordinary skill in the art would not have applied the alleged modification taught by *Patani* to compound 401470-74-4 because, as explained above, this compound has not been identified in WO 2002/014272 as a lead compound.

f. The Office has not provided a reason why one of ordinary skill in the art would have carried out the modifications proposed by the Office with a with a reasonable expectation of success

As mentioned above, the Office needs to provide "a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention." *Takeda*, 83 U.S.P.Q.2d at 1174. The Office has failed to supply such a showing. The Office seems to argue that because *Patani* teaches that the sulfonemoiety is a bioisostere of the carbonyl group, such knowledge would have motivated one of ordinary skill in the art to make the substitution of the carbonyl group for sulfone in compound 401470-74-4. Office Action at 6. However, the Office has ignored *Patani's* results showing that in every instance when the carbonyl group was substituted with sulfone, the activity of the resulting compound decreased. For

example, the replacement of the carbonyl in an antagonist of an LTB_4 receptor with sulfone reduced the inhibitory activity of the compound from 85% to 79%. *Patani* at Table 39, p. 3167. Also, the replacement of the carbonyl group in an euglycemic agent by a sulfone group reduced the activity of the compound from 100% to 69%. *Id.* at Table 41, p. 3168.[1] Therefore, contrary to the Office's assumption, the teachings in *Patani* would not have led one of ordinary skill in the art to replace a carbonyl group by a sulfone group in compound 401470-74-4 because of the expectation that such modification would have led to compounds with less biological activity than that of compound 401470-74-4.

In summary, it remains unclear: a) why one of ordinary skill in the art would have selected compound 401470-74-4 from those disclosed in WO 2002/014272 for further modification and b) why one of ordinary skill in the art would have modified compound 401470-74-4 as suggested by the Office. Accordingly, the Office has not met its burden to show a *prima facie* case of obviousness. Thus, Applicants respectfully request that this rejection be withdrawn.

IV. Claim Objections

The Office stated that "[t]he elected compound appeared to be obvious over the prior art" and that, "[t]herefore, the provisional election of species was given effect." Office Action at 4. On this basis, the Office objected to claims 1-10, 20 and 21 for containing non-elected subject matter "consist[ing] of compounds of Formula I that are not the elected species." *Id.*

[1] The results in *Patani's* Table 40 do not involve the replacement of a carbonyl group by a sulfone group and are not relevant to the present analysis.

In view of the foregoing remarks, Applicants submit that neither the elected species nor the pending claims are obvious over the cited art. Accordingly, Applicants respectfully request that this objection be withdrawn.

V. Conclusions

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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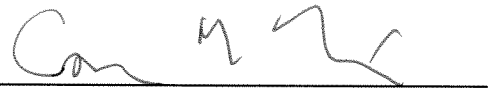
By: 

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Dated: October 22, 2008